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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/663,264	09/16/2003	Nicholas W. Warne	22058-544 (AM100664)	1450

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EXAMINER	
HISSONG, BRUCE D	
ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 06/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/663,264	WARNE ET AL.	
	Examiner	Art Unit	
	Bruce D. Hissong, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-12,17-26 and 28-55* is/are pending in the application.

4a) Of the above claim(s) *42-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-12,17-26,28-41 and 53-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *3/7/2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

1. The Applicant's response was received on 3/7/2006 and has been entered into the record.

2. The text of those sections of Title 35, U.S.C. not included in this action can be found cited in full, in the previous office action mailed on 12/7/2005.

3. The Applicant's, in the response received on 3/7/2006, have cancelled claims 1-4, 13-16, and 27, and have added new claims 53-55.

4. Claims 5-12, 17-26, and 28-55 are currently pending, and claims 5-12, 17-26, 28-41, and 53-55 are the subject of this Office Action.

Drawings

The objection to the drawings, as set forth on p. 3 of the Office Action mailed on 12/7/2005, is maintained. While the amended drawings do favorably resolve the issue of overlapping figure labels, the amended figure itself it too dark, and the individual drug layers of the figure are not discernable from each other.

Specification

The objection to the specification, as set forth on p. 3 of the Office Action mailed on 12/7/2005, is maintained. Applicants have not addressed the issue of improperly designated trademarks in the specification.

Claim Objections

Objections withdrawn

1. Objection to claim 9 as self-referential, as set forth on p. 3 of the Office Action mailed on 12/7/2005, is withdrawn in response to Applicant's amendment to the claim.

2. Objection to claims 10-12 and 16-18 for depending from an objected base claim, as set forth on p. 3 of the Office Action mailed on 12/7/2005, is withdrawn in response to the Applicant's amendment to claim 9 and cancellation of claim 16.

3. Objection to claim 1, as set forth on p. 4 of the Office Action mailed on 12/7/2005, is withdrawn in response to the cancellation of the claim.

Objections maintained and new objections necessitated by Applicant's amendments

4. Objection to claim 5, as set forth on p. 4 of the Office Action mailed on 12/7/2005, is maintained. The Examiner feels that the syntax and wording of the claim would be improved by including numbering or lettering for each part of the claimed composition.

5. Claim 18 is objected to for depending from a cancelled claim. Claim 18, as currently written, depends from claim 16, which was cancelled in the amendment received on 3/7/2006.

6. The Examiner suggests amending claim 9 to read "The pharmaceutical composition.....".

Claim Rejections - 35 USC § 112, first paragraph – enablement

Rejections withdrawn

1. Rejection of claims 1-4, 13-15, and 27 under 35 USC § 112, first paragraph, regarding lack of enablement for a pharmaceutical composition comprising any bioactive peptide, as set forth on p. 4-5 of the prior Office Action mailed on 12/7/2005, is withdrawn in response to Applicant's cancellation of the claims.

2. Rejection of claims 16 and 28-41 under 35 USC § 112, first paragraph, regarding lack of enablement for a pharmaceutical composition comprising any interleukin (IL)-11 polypeptide, as set forth on p. 4-5 of the prior Office Action mailed on 12/7/2005, is withdrawn in response to Applicant's cancellation of claim 16, and the amendment of claim 28 to read on a pharmaceutical composition comprising a polypeptide comprising the amino acid sequence of a human IL-11 peptide. However, the rejection is maintained, in part, as seen in part 4 below.

3. Rejection of claims 1-26 and 36 under 35 USC § 112, first paragraph, regarding lack of enablement for a pharmaceutical composition comprising any glidant other than talc, as set forth on p. 6-7 of the prior Office Action mailed on 12/7/2005, is withdrawn in response to Applicant's cancellation of claims 1-4, 13-16, and 27, as well as the Applicant's arguments that other glidants are well-known in the art and that the specification provides concentrations and specific examples of glidant other than talc.

Rejections maintained and/or necessitated by amendment

4. Claims 5-12, and 17-26 remain rejected under 35 USC § 112, first paragraph, regarding lack of enablement for a pharmaceutical composition comprising any interleukin (IL)-11 polypeptide, as set forth on p. 4-5 of the prior Office Action mailed on 12/7/2005. The Applicant's have amended the claims to read on a pharmaceutical composition comprising human IL-11, and argue that because human IL-11 polypeptides were well-known at the time of the earliest priority date of the instant application, the specification is enabling for compositions comprising human IL-11. These arguments have been fully considered and are not found persuasive. While the Examiner acknowledges that human IL-11 polypeptides were known in the art at the earliest effective filing date of the instant application, the specification is not enabling for the breadth of the claims. As currently amended, the preamble of claim 5 still reads on a pharmaceutical composition comprised of any IL-11 polypeptide. Given the broadest reasonable interpretation, the amended claims could read on a pharmaceutical composition comprising a human IL-11 polypeptide and further comprising any other IL-11 polypeptide. For the reasons set forth on p. 4-5 of the prior Office Action mailed on 12/7/2005, the specification is not enabling for a pharmaceutical composition comprised of any IL-11 polypeptide other than human IL-11.

Claim Rejections - 35 USC § 112, first paragraph – written description

Rejections withdrawn

1. Rejection of claims 1-4, 13-15, and 27 under 35 USC § 112, first paragraph, regarding lack of written description for a pharmaceutical composition comprising any bioactive peptide, as set forth on p. 7-8 of the prior Office Action mailed on 12/7/2005, is withdrawn in response to Applicant's cancellation of the claims.

2. Rejection of claims 16-26 and 28-41 under 35 USC § 112, first paragraph, regarding lack of written description for a pharmaceutical composition comprising any IL-11 polypeptide, as set forth on p. 8-9 of the prior Office Action mailed on 12/7/2005, is withdrawn in response to Applicant's cancellation of claim 16 and the amendment of claim 28 to read on a pharmaceutical composition comprising a polypeptide comprising the amino acid sequence of a human IL-11 peptide. However, the rejection is maintained, in part, as seen in part 3 below.

Rejections maintained and/or necessitated by amendment

3. Claims 5-12 and 17-26 remain rejected under 35 USC § 112, first paragraph, regarding lack of written description for a pharmaceutical composition comprising any IL-11 polypeptide, as set forth on p. 8-9 of the prior Office Action mailed on 12/7/2005. The Applicant's have amended the claims to read on a pharmaceutical composition comprising human IL-11, and argue that because human IL-11 polypeptides were well-known at the time of the earliest priority date of the instant application, the specification provides adequate written description for the claimed genus of human IL-11 polypeptides. These arguments have been fully considered and are not found persuasive. As stated above in the 35 U.S.C. 112 first paragraph enablement rejection, the preamble of claim 5 still reads on a pharmaceutical composition comprised of any IL-11 polypeptide. Given the broadest reasonable interpretation, the amended claims could read on a pharmaceutical composition comprising a human IL-11 polypeptide and further comprising any other IL-11 polypeptide. Because the claims, as currently amended, read on a pharmaceutical composition comprising any IL-11 polypeptide,

the specification does not provide adequate written description for the claimed genus of IL-11 polypeptides for the reasons set forth on p. 8-9 of the prior Office Action of 12/7/2005.

Claim Rejections - 35 USC § 112, second paragraph

Rejections withdrawn

1. Rejection of claims 1-4 and 27 under 35 USC § 112, second paragraph, for being indefinite for failing to define the metes and bounds of the term "bioactive", as set forth on p. 9 of the prior Office Action mailed on 12/7/2005, is withdrawn in response to Applicant's cancellation of the claims.

Claim Rejections - 35 USC § 103

Rejections withdrawn

1. Rejection of claims 1-22, 25, and 27-41 under 35 USC § 103, as being obvious in view of Savastano *et al* (US 5,681,584), as set forth on p. 9-12 of the prior Office Action mailed on 12/7/2005, is withdrawn in response to Applicant's cancellation of claims 1-4, 13-16, and 27, and in view Applicant's arguments regarding the remaining claims (see below). Savastano *et al* teaches a controlled release drug delivery device comprised of a core containing a bioactive therapeutic agent, a first coating layer, and enteric coating layer, and second coating layer. Savastano *et al* also discloses that the bioactive therapeutic agent can consist of a polypeptide or protein, and specifically recites interleukins and interferons as bioactive agents that can be used. Furthermore, the controlled release drug delivery device taught by Savastano *et al* shares all of the features of the invention of the instant application regarding the different coating layers and the composition of said layers (see p 10-11 of the Office Action of 12/7/2005). In the response received on 3/7/2006, the Applicants argue that the claims in question are not obvious over Savastano *et al*, because IL-11 has properties that distinguish it from other proteins, including other interleukins and cytokines, and therefore there would be no expectation that constructing an IL-11-containing formulation with the formulations disclosed in Savastano *et al* would be successful. These arguments have been fully considered and are found persuasive. The Examiner agrees that Savastano *et al*, by itself, does not provide the

motivation or reasonable expectation of success in creating the claimed pharmaceutical composition comprising human IL-11.

2. Rejection of claims 23, 24, and 26 under 35 USC § 103, as being obvious in view of Savastano *et al* (US 5,681,584) and further in view of Porter, as set forth on p. 12 of the prior Office Action mailed on 12/7/2005, is withdrawn in response to Applicant's arguments that claims 23, 24, and 26 depend directly from claim 5, which was rejected in view of Savastano *et al* (see above), and that Savastano *et al* does not provide adequate motivation or a reasonable expectation of success in creating the composition of the instant invention (see above). These arguments have been fully considered and have been found persuasive for the reasons stated above.

New grounds of rejection necessitated by amendment

3. Claims 5-12, 17-22, 25, 28-41, and new claims 53-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Savastano *et al* (US 5, 681,584 – cited in the Office Action mailed on 12/7/2005) in view of Greenwood-van Meerveld *et al* (2001, *J. Pharmacol. Exp. Ther.*, Vol. 299(1), p. 58-66 – referred to hereafter as "Greenwood"). The claims of the instant application are drawn to a delayed-release, oral dosage pharmaceutical composition, comprising human IL-11, and further comprising at least one binder, at least one plasticizer, at least one glidant, and a methacrylic acid copolymer. In some embodiments, the human IL-11 is enveloped by a first sealing coat, an enteric coating layer, and a second sealing coat. Savastano *et al* describe a controlled release drug delivery device which consists of a core containing the bioactive therapeutic agent, and a first coating layer (called a "delay jacket"), an enteric coating layer (termed a "semi-permeable membrane"), and a second coating layer (referred to as the "enteric" layer in Savastano *et al*, but having the features of the claimed second coating layer of the instant application).

Specifically, Savastano *et al* teaches a core which can be comprised of active agents which can include proteins and polypeptides, including interferons and interleukins (column 6, lines 33-39). The core is further comprised of several pharmaceutical excipients, including carbohydrates and amino acids (column 7, lines 24-30). In particular, the inclusion of sucrose (column 7, line 42) and the amino acid methionine (column 7, line 44) are taught by Savastano

et al. Additionally, Savastano *et al* also teaches the inclusion of the surfactant polysorbate 80 in the pharmaceutical composition (column 7, lines 64-65).

Savastano *et al* also teach the use of:

i. at least one binder, ethylcellulose or hydroxypropylmethylcellulose (HPMC – column 8, lines 3-4)

ii. at least one plasticizer (polyethylene glycol or polypropylene glycol – column 7, lines 46-47, column 8, lines 14-17, and column 9, lines 31-32)

iii. at least one glidant (talc – column 7, line 54)

iv. a methacrylic acid copolymer (column 9, line 66 and column 10, lines 13-16), applied as a dispersion (column 10, lines 46-57).

Furthermore, Savastano *et al* teaches a biologically therapeutic agent in a core comprised of the excipients described above, and also surrounded by an inner coating layer, an enteric layer, and an outer coating layer. Although the terminology used is not identical to that of the instant application, the both the function and the composition of the layers is the same. The invention of Savastano et al also shares a number of other features with the invention of the instant application. Both Savastano *et al* and the instant application teach a pharmaceutical core surrounded by an inner layer, and both specify that the inner layer may be comprised of HPMC (column 8, lines 34-41 and column 9, lines 28-32). Savastano *et al* and the instant application also both teach a middle layer comprised of a methacrylic acid copolymer (column 9, line 66, and column 10, lines 13-16). Specifically, Savastano *et al* and the instant application both specify the use of the methylacrylic acid copolymer EUDRAGIT (column 10, lines 46-57). Finally, both Savastano *et al* and the instant application claim the use of an outer coating layer comprised of HPMC (column 11, line 36), and teach the formulation as a tablet (see Examples 1-4).

Savastano *et al* teaches the bioactive agent can be any protein or polypeptide, including interleukins or interferons, but is silent regarding the inclusion of human IL-11 in the pharmaceutical composition.

Greenwood teaches oral administration of recombinant human IL-11 (rhIL-11) to rats with intestinal inflammation. Specifically, Greenwood teaches oral administration of rhIL-11 that was coated with an enteric polymer that allows the rhIL-11 to pass through the stomach and be released in the intestines (p. 59, 2nd column, 1st full paragraph). Greenwood also teaches that rhIL-11 administered in this manner is effective in relieving symptoms of chronic intestinal inflammation (see results - p. 60–64), indicating that functional rhIL-11 was effectively delivered by the method of orally administering rhIL-11 with an enteric coat.

It would have been obvious to a person of ordinary skill in the art, at the time the instant application was filed, to combine the teaching of Savastano *et al* and Greenwood to practice the claimed invention of the instant application. By teaching a delayed-release drug delivery device for delivering proteins or polypeptides to the intestinal tract, Savastano *et al* would provide the motivation to coat a core containing proteins or polypeptides with the coating layers of the claimed invention. Greenwood, by teaching that rhIL-11 can be formulated for delayed release in the intestine by employing an enteric coat, would provide the motivation to incorporate rhIL-11 into the composition taught be Savastano *et al*.

The claims of the instant invention are drawn to the inclusion of several pharmaceutical excipients at various final percentages. As described above, Savastano *et al* teaches the use of a carbohydrate, amino acids such as methionine, methacylic acid copolymers, HPMC, and talc. Savastano *et al* is silent in regards to the final percentage of each excipient in the final composition. However, optimization of excipients is common in the pharmacological arts. A person of ordinary skill in the art would have both the movitation, and the technical expertise, to optimize the excipients listed above, and would have a reasonable expectation of success in doing so and arriving at the concentrations of the instant invention.

The claims of the instant invention are also drawn to a pharmaceutical composition, as described above, in capsule form. Although Savastano *et al* teaches a composition in tablet form and is silent in regards to a composition in capsule form, pharmaceuticals in capsule form are well-known in the art. It would require routine optimization for a skilled artisan to adapt the composition of the instant invention to capsule form, and the skilled artisan would have both the motivation, and the technical expertise to do so with a reasonable expectation of success.

In summary, a person of ordinary skill in the art, at the time the invention was made, would have both the motivation and a reasonable expectation of success in creating the invention of the instant application by following the teachings of Savastano *et al* and Greenwood. Savastano *et al* teaches a delayed delivery device for intestinal delivery of proteins and polypeptides that shares the features of the invention of the instant application. Greenwood teaches that human IL-11 is capable of being formulated in an enteric coating for intestinal release, and is biologically functional after oral administration in this manner. Thus, in view of these teachings, it would be obvious to one of ordinary skill in the art to incorporate human IL-11 into the delayed-release device of Savastano *et al*.

4. Claims 23, 24, and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Savastano *et al*, in view of Greenwood-van Meerveld *et al* ("Greenwood"), and further in view of Porter (In Remington's Pharmaceutical Sciences, 19th Ed. 1995, Chapter 93, p. 1653, 1st column, 9th paragraph – cited in the Office Action mailed on 12/7/2005). The claims of the instant invention are drawn to a pharmaceutical composition, described above, which contains triethyl citrate as a plasticizer. The teachings of Savastano *et al* and Greenwood are described above. Savastano *et al* and Greenwood do not teach the use of triethyl citrate as a plasticizer. However, Porter does teach that plasticizers are often incorporated into pharmaceutical compositions, and lists triethyl citrate as an accepted plasticizer.

Therefore, a person of ordinary skill in the art, at the time the invention was made, would have been motivated to combine the teachings of Savastano *et al* and Greenwood with those of Porter to practice the invention of the instant application as claimed. The motivation to follow the teachings of Savastano *et al* and Greenwood is described above. By teaching that triethyl citrate is a commonly used plasticizer, Porter would provide the motivation to incorporate triethyl citrate into the pharmaceutical composition of the instant invention. Thus, by following the teachings of Savastano *et al*, Greenwood, and Porter, a person of ordinary skill in the art would have both the motivation to create the composition for delayed drug delivery as claimed in the instant invention, but also a reasonable expectation of success in doing so.

Double Patenting

1. Provisional rejection of claims 1-4, 13-16, and 27 on the grounds on nonstatutory double patenting over claims 13, 15, 20, 22-23, and 28 of copending Application No. 10/360,906, is withdrawn in response to the cancellation of the claims.

2. Provisional rejection of claims 5, 17-20, 28-31, and 38-39 on the grounds of nonstatutory double patenting over claim 13 of copending Application No. 19/360,906, is maintained. In the response received on 3/7/2006, the Applicants note that Application No. 10/360,906 is not yet allowed and will address any double-patenting issues with respect to the claims of the instant application and the claims in the conflicting application upon the indication of allowable subject matter in the conflicting application. The Examiner also notes that claims 15, 20, 22-23 and 28 were inadvertently listed as conflicting with the indicated claims of the instant application. Only claim 13 of Application No. 10/360,906 is deemed to conflict with the claims of the instant application.

Conclusion

No claim is allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571) 272-3324. The examiner can normally be reached M-F from 8:30am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BDH
Art Unit 1646

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PRIMARY EXAMINER